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# Ambiphilic Dual Activation Role of a Task-Specific Ionic Liquid: 2-Hydroxyethylammonium Formate as a Recyclable Promoter and Medium for the Green Synthesis of β-Nitrostyrenes

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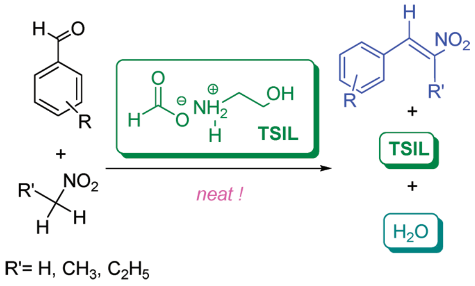

A cost-effective task-specific ionic liquid, 2-hydroxyethyl ammonium formate, efficiently promotes the condensation of nitroalkanes with various aldehydes to produce β-nitrostyrenes in high to excellent yields at room temperature. This reaction does not involve any hazardous organic solvent and toxic catalyst. The ionic liquid is recovered and recycled for subsequent reactions. In addition, a novel mechanism has been proposed invoking ambiphilic dual activation influence of the ionic liquid.

As the nitro group is a strong electron-withdrawing group, nitroalkenes are versatile synthetic reagents. For example, conjugate addition,[1a] Diels−Alder reaction,[1b] and 1,3-dipolar addition[1c] using nitroalkenes are powerful methods for carbon−carbon bond formation. Moreover, since after these reactions the nitro groups can be converted into various functional groups, nitroalkenes have become important intermediates in organic synthesis, and several strategies for their synthesis are known. Henry reaction (condensation of carbonyl compounds with nitroalkanes followed by β-elimination of the resulting 2-nitro alcohols) is one of the well-, alcoholic sodium hydroxide solution and concentrated hydrochloric acid,[2a] microwave techniques (900 W) in ammonium acetate,[2b] ultrasound (US)/$NH_4OAc$/HOAc,[2c] direct nitration of alkenes with copper(II) tetrafluoroborate and $NaNO_2$ in acetonitrile,[2d] Clayfen by MW irradiation (100−110 °C),[2e] and ceric ammonium nitrate (CAN)[2f] have been utilized to obtain nitroalkenes. In addition, various heterogeneous catalysts such as zeolite,[3a] aminopropyl-functionalized silicas (APS),[3b] FDU-ED (diamino-functionalized mesostructured polymers),[3c] and MCM-41 silica[3d] have been employed for the synthesis of nitroalkenes starting from aromatic aldehydes and nitroalkanes. However, most of the reported methods have one or more of the following drawbacks: for example, use of expensive reagents and volatile organic solvents, long reaction times, low yields of products, complicated reaction assembly, and tedious work-up, etc.

In view of the projected benefits of ionic liquids (ILs) for organic transformations for sustainable development such as environmental compatibility, reusability, greater selectivity, operational simplicity, noncorrosiveness, and ease of isolation,[4] we were attracted toward the use of ILs. A survey of the literature indicated that there is no report aimed at the synthesizing of β-nitrostyrenes utilizing ionic liquids. Herein, we report the first utilization of a low cost and task-specific ionic liquid, namely 2-hydroxyethylammonium formate (2-HEAF),[5] in developing an environmentally improved route to β-nitrostyrene derivatives.

To examine the effect of 2-HEAF as an ionic liquid, the reaction of nitromethane with benzaldehyde under neat condition and at room temperature was considered for a model study. An initial screening was done to obtain maximum conversion to the product in the shortest period. The progress of the reactions was monitored by TLC taking into consideration the complete consumption of aldehyde. The reactants (1 mmol of benzaldehyde and 1 mmol of nitromethane) were obtained unchanged even after 48 h stirring in ethanol without addition of 2-HEAF at rt and also under reflux conditions (Table 1, entries 1 and 2). The lack of formation of any significant amount of the desired product without using the IL indicated the specific role of 2-HEAF in imparting the catalytic property. To optimize the quantity of IL required, the reaction was carried out in the presence of 1, 0.5, and 5 mL of 2-HEAF under neat conditions and room temperature. In these cases, the desired

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**TABLE 1. Catalytic Effect of 2-HEAF on the Synthesis of $\beta$-Nitrostyrene by the Reaction of Nitromethane with Benzaldehyde under Various Conditions[a]**

| entry | IL (ml) | solvent | $T$ (° C) | time (h) | yield[b] (%) |
|---|---|---|---|---|---|
| 1 | 0.0 | EtOH | rt | 48 | NR[c] |
| 2 | 0.0 | EtOH | reflux | 48 | NR |
| 3 | 1.0 | neat | rt | 0.5 | 91 |
| 4 | 0.5 | neat | rt | 3.0 | 45 |
| 5 | 5.0 | neat | rt | 1.0 | 88 |
| 6 | 1.0 | neat | 50 | 1.5 | 90 |

[a] Reaction conditions: benzaldehyde (1 mmol), nitromethane (1 mmol), IL under neat conditions. [b] Yields refer to the pure isolated products. [c] NR: no reaction.

$\beta$-nitrostyrene was formed in 91, 45, and 88% isolated yields after 30, 180, and 60 min, respectively (Table 1, entries 3−5).

Our several attempts to scale down the amount of IL were unsuccessful. As a proof of principle experiment, we first started with 0.1, 0.2, and 0.5 mL which equal with ~1.1, 2.2, and 5.5 mmol of IL, respectively ($M_w$ = 107.11 g/mol; density = 1.204 g/cm3).[5] In all cases, the main problem that we met was the formation of a very gummy mixture resulting in a very low conversion of starting materials to the desired products. Using at least 1 mL of IL, we obtained the best Additionally, further increase in the reaction temperature (up to 50 °C) resulted in no considerable decrease in the reaction time or no increase in the reaction yield (Table 1, entry 6). Thus, the use of 1 mL of 2-HEAF at room temperature was considered as the optimal amount keeping in view the feasibility of handling the IL for small-scale reactions.

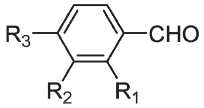
To establish the generality of this IL-promoted $\beta$-nitrostyrene formation, various aryl, heteroaryl, and polycyclic aromatic aldehydes were treated with nitroalkanes (nitromethane, nitroethane, and 1-nitropropane), and the results are summarized in Table 2.

It was found that the length of the alkyl chain of nitroalkanes has a significant influence on their efficiency as nucleophiles and, therefore, on the reaction time and the yields. We observed that nitromethane shows a particular reactivity toward aldehydes, and in contrast, with an increase of the alkyl chain length in nitroethane and 1-nitropropane, the reaction time increases (compare entries 2 with 16 or 23 with 24 in Table 2), possibly due to the more sterics hindering the ability of them to react with the aldehydes.

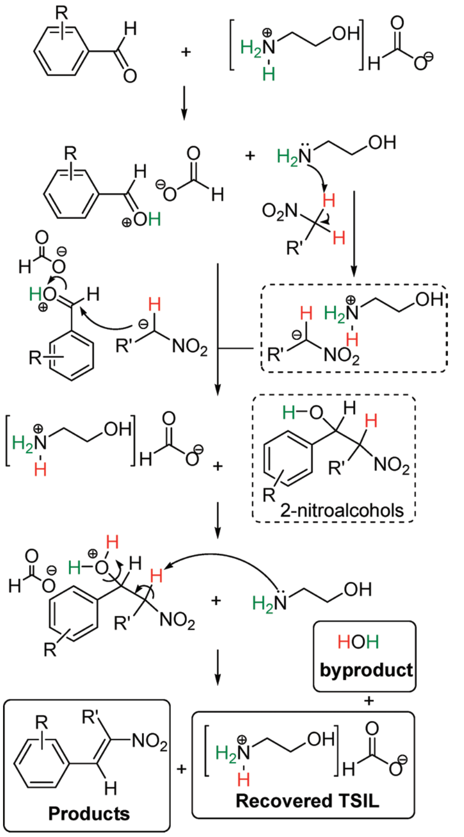
In all cases, the reaction proceeded smoothly at rt and under neat conditions to afford the corresponding $\beta$-nitrostyrenes in excellent yields (80−97%) in reaction times ranging from 0.5 to 6.5 h. Also notably, the reaction is compatible with a variety of functional groups such as hydroxy, halogen, alkoxy, and nitrile.

The dramatic influence of 2-HEAF in promoting the reaction has been envisaged through the mechanistic proposal depicted in Scheme 1. In explaining how this ionic liquid leads the condensation reaction of aryl aldehydes and

**TABLE 2. Synthesis of $\beta$-Nitrostyrenes Promoted by 2-Hydroxyethylammonium Formate**

| Entry | Aldehyde | R'-NO$_2$ | Time/h | Yield % | Mp (°C) | Reported |
|---|---|---|---|---|---|---|
| |  | R' | | | | |
| 1 | $R_1,R_2,R_3$= H | $CH_3$ | 0.5 | 91 | 58 | 56-58[6] |
| 2 | $R_1,R_2$= H; $R_3$= 4-Me | $CH_3$ | 0.8 | 95 | 103 | 102-104[7] |
| 3 | $R_1,R_2$= H; $R_3$= 4-OMe | $CH_3$ | 1.1 | 94 | 87 | 86-87[8] |
| 4 | $R_1,R_2$= H; $R_3$= 4-$NO_2$ | $CH_3$ | 0.7 | 97 | 106 | 106-108[9] |
| 5 | $R_1,R_2$= H; $R_3$= 4-Br | $CH_3$ | 2 | 95 | 147 | 148-150[10] |
| 6 | $R_1,R_2$= H; $R_3$= 4-OH | $CH_3$ | 3 | 92 | 169 | 168-169[6] |
| 7 | $R_1,R_2$= H; $R_3$= 4-CN | $CH_3$ | 0.7 | 97 | 186 | 186-188[11] |
| 8 | $R_1,R_2$= H; $R_3$= H | $C_2H_5$ | 3 | 90 | 63 | 64-65[6] |
| 9 | $R_1,R_2$= H; $R_3$= 4-Me | $C_2H_5$ | 4.1 | 95 | 54 | 53-54[12] |
| 10 | $R_1,R_2$= H; $R_3$= 4-OMe | $C_2H_5$ | 2.5 | 91 | 45 | 44-45[12] |
| 11 | $R_1,R_2$= H; $R_3$= Cl | $C_2H_5$ | 2.1 | 90 | 86 | 84-85[12] |
| 12 | $R_1,R_2$= H; $R_3$= 4-CN | $C_2H_5$ | 2.5 | 93 | 109 | 103-108[11] |
| 13 | $R_1,R_2$= H; $R_3$= 4-OH | $C_2H_5$ | 5.5 | 88 | 124 | 124-125[6] |
| 14 | $R_1,R_2$= H; $R_3$= 4-F | $C_2H_5$ | 4 | 91 | 66 | 64-66[13] |
| 15 | $R_1,R_2$= H; $R_3$= 4-$NO_2$ | $C_2H_5$ | 2.2 | 95 | 114 | 113-114[3b] |
| 16 | $R_1,R_2$= H; $R_3$= 4-Me | $C_3H_7$ | 6.5 | 80 | 32 | 32-33[12] |
| 17 | $R_1,R_2$= OMe; $R_3$= H | $CH_3$ | 1.3 | 94 | 85 | 84-85[8] |
| 18 | $R_1,R_3$= Cl; $R_2$= H | $CH_3$ | 3.5 | 92 | 115 | 115-117[14] |
| 19 | $R_1,R_2$= OMe; $R_3$= H | $C_2H_5$ | 1.5 | 90 | 78 | 78-79[8] |
| 20 | Furan-2-carbaldehyde | $CH_3$ | 0.6 | 95 | 74 | 72-74[15] |
| 21 | Furan-2-carbaldehyde | $C_2H_5$ | 1.2 | 96 | 47 | 46-47[16] |
| 22 | 1-Naphthaldehyde | $CH_3$ | 2.5 | 91 | 84 | 84-86[14] |
| 23 | 4-(5-Bromopentyloxy) benzaldehyde | $CH_3$ | 6 | 90 | 96 | -- |
| 24 | 4-(5-Bromopentyloxy) benzaldehyde | $C_2H_5$ | 17 | 65 | Oil | -- |
| 25 | 4-(12-Bromododecyloxy) benzaldehyde | $C_2H_5$ | 20 | 60 | 53-54 | -- |

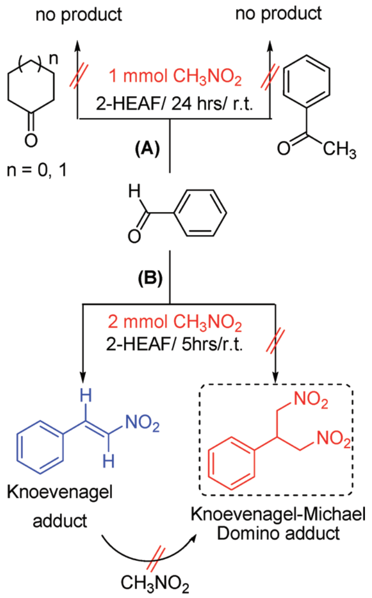
**SCHEME 1. Dual Catalytic Role of 2-HEAF in Promoting the Reaction of Nitroalkanes with Aryl Aldehydes**



nitroalkanes to $\beta$-nitrostyrene derivatives in a sequential one-pot route, we postulate that the structure of 2-HEAF with a specific feature (bearing hydroxy group, ammonium acidic moiety, and formate anion) may have a subtle influence on the mechanism of the reaction.

Obviously, the acidic part of 2-HEAF can protonate the oxygen atom of the aldehydes. On the other hand, we believe that the transiently generated ethanol amine can act as a base and therefore deprotonates C−H acids (nitroalkanes), affording active nitro enolates. These nucleophilic intermediates can subsequently attack to the protonated aldehydes affording 2-nitro-1-phenyl alcohols. This part of the reaction is called the Henry reaction, which is normally a base-catalyzed C−C bond-forming reaction between nitroalkanes and aldehydes. Also notably, if acidic protons are available (i.e., when protic solvent or catalyst), 2-nitro alcohols tend to eliminate water to give nitroalkenes. It has to be noted that during the course of our investigations, we did not observe any evidence of the formation of 2-nitro alcohols (by TLC monitoring), and only corresponding nitroalkenes were obtained as the final products in a fast and one-pot pathway. The IL was recovered, and water was obtained as the only byproduct of the reactions. These results allowed us to propose a mechanism for this ionic liquid-promoted one-pot condensation reaction of various aryl, heteroaryl, and polycyclic aromatic aldehydes with nitroalkanes, as depicted in Scheme 1. We believe that this reaction proceeds through a one-pot sequential fashion affected by a dual dramatic influence of 2-hydroxyethylammonium formate as a cost-effective and task-specific ionic liquid acting as promoter and the reaction medium.

**SCHEME 2**



Additionally, to elucidate how the structural variation of carbonyl group will affect its reactivity toward nitroalkanes under the developed conditions, we studied the condensation reaction of nitroalkanes with cyclic and acyclic ketones under conditions similar to those of aldehydes. In contrast with the aldehydes, any effort to obtain the condensation adducts of the reaction of nitroalkyl anion with cyclohexanone, cyclopentanone, or acetophenone was unsuccessful (Scheme 2A). This is presumably, in part, due to the lower reactivity of ketones in nucleophilic addition reactions compared to aldehyes.

Since $\beta$-nitrostyrenes are known as the versatile Michael acceptors, we were also interested in investigating whether the structure of final products of this IL-promoted reaction can be complicated by using an excess amount of nitroalkanes and lead to the Michael adducts. To investigate this, an attempted control experiment was allowed to proceed under the developed conditions utilizing 1 mmol of benzaldehye, 2 mmol of nitromethane, and 1 mL of 2-HEAF (Scheme 2B). It was found that even in the presence of excess nitromethane, only the Knoevenagel condensation reaction of nitromethyl anion with benzaldehye affording (*E*)- $\beta$-nitrostyrene occurs and no evidence (TLC monitoring) was found for the formation of Michael adducts of (*E*)- $\beta$-nitrostyrene with the second molecule of

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**TABLE 3. Comparative Results for the Synthesis of β-Nitrostyrene Using the Reported Methods versus the Present Method (Entry 6)**

| entry | reactants | | conditions | time (min) | yield (%) |
|---|---|---|---|---|---|
| 1 | benzaldehyde | $CH_3NO_2$ | MW(900 W)/$NH_4OAc$ | 8 | 80[2b] |
| 2 | benzaldehyde | $CH_3NO_2$ | MCM-41 silica catalyst/90 °C | 60 | 5−98[3d] |
| 3 | benzaldehyde | $CH_3NO_2$ | aminopropyl silica catalyst (APS)/90 °C | 120 | 95[3b] |
| 4 | styrene | Clayfen or Clayan | oil bath or MW/100−110 °C | 3−15 | 68[2e] |
| 5 | styrene | $NaNO_2$ | $CuO\cdot HBF_4,I_2$/rt | 420 | 47[2d] |
| 6 | benzaldehyde | $CH_3NO_2$ | 2-HEAF(IL)/rt | 30 | 91 |

nitromethane. This is probably due to the insolubility of the β-nitrostyrene in 2-HEAF as the reaction medium.

Finally, to assess the capability of the present method with respect to the reported methods for the preparation of β-nitrostyrenes, the synthesis of β-nitrostyrene using 2-HEAF was compared with some of the reported methods (Table 3).

As is clear from Table 3, the present procedure involving avoidance of organic volatile solvents and toxic catalysts, room-temperature conditions, and the use of an inexpensive ionic liquid is very simple and convenient.

In general, the reactions were very clean and high yielding, they proceed without introducing any acid, base, or metal catalyst, and no side products were detected in any reaction. All products were crystalline compounds (except entry 24) and were easily identified by their melting points and spectroscopic data.

Nitroalkene derivatives are of intense attention since they are used as important intermediates in organic synthesis, and thus, an efficient procedure for their synthesis is of high importance. The present procedure using a cost-effective ionic liquid, 2-HEAF, in place of conventional catalysts, provides a clean, high-yielding, one-pot synthesis of nitroalkene derivatives through a condensation process. Significantly, the formation of a side product, 2-nitro-1-phenyl alcohols, was virtually eliminated.

The other advantages of this procedure are the use of no hazardous organic solvent in the reaction and the reusability of ionic liquids. The recovered ionic liquid was reused three times without addition of extra ionic liquid and significant loss of activity. The ease of preparation from commercially available and low-cost starting materials, high conductivity, powerful solvating ability, and low melting point make 2-HEAF a promising task-specific room-temperature ionic liquid. We believe that the low cost and the experimental simplicity of the method gives this green ionic liquid-promoted procedure great potential, and it may find potential importantly, can compliment the existing chemical strategies. Encouraged by these results, we are pursuing further application of a series of cost-effective and task-specific ionic liquids for such useful transformations.

## Experimental Section

**General Experimental Procedure for the Synthesis of β-Nitrostyrenes. Representative Procedure for (*E*)-1-(4-Cyanophenyl)-2-nitropropene (Table 2, Entry 12).** In a 25 mL round-bottom flask, 4-cyanobenzaldehyde (0.131 g, 1 mmol), nitroethane (0.075 g, 1 mmol), and 2-HEAF[5] (1.204 g, 1 mL, 11.2 mmol) were mixed together and stirred for 2.5 h at room temperature until completion (TLC) of the reaction. Then, addition of water (5 mL) to the flask led to the immediate formation of the crude solid which was recrystallized to furnish pale-yellow crystals (mp 109 °C) of (*E*)-1-(4-cyanophenyl)-2-nitropropene (0.174 g, 93%). The spectroscopic data ($^1H$ NMR, and $^{13}C$ NMR) are in good agreement with the reported values.[11] The remaining ionic liquid was rinsed with ethyl acetate, dried under a vacuum, and reused for three runs after which a fresh ionic liquid was added to compensate the loss during washing by ethyl acetate. This procedure was followed for all the reactions listed in Table 2. Although this procedure was described with a 1 mmol scale, 10 mmol scale reactions also provided uniform results.

Many of these products are known compounds and were easily identified by comparison of their spectroscopic data and mp's with those reported (refs in Table 2). The unknown compounds were properly characterized by their spectroscopic (IR, $^1H$ NMR, $^{13}C$ NMR, and HRMS) data.

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**Supporting Information Available:** Copies of $^1H$ and $^{13}C$ NMR, FT-IR, and HRMS of all unknown compounds in Table 2. This material is available free of charge via the Internet at http://pubs.acs.org.